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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,158	07/28/2000	Raghunath Vitthal Chaudhari	5728	2931
7590	03/23/2004			
Arlene J. Powers Samuels Gauthier & Stevens LLP 225 Franklin Street Suite 3300 Boston, MA 02110			EXAMINER OH, TAYLOR V	
			ART UNIT 1625	PAPER NUMBER

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/628,158	Applicant(s) CHAUDHARI ET AL.	
	Examiner Taylor Victor Oh	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 8-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2 and 8-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/4/2004 has been entered.

The Status of Claims :

Claims 1-2 and 8-21 are pending.

Claims 1-2 and 8-21 have been rejected.

Claim Objections

Claim 21 is objected to because of the following informalities: the phrase "inclaim 1" is recited. There is no gap between "in " and "claim 1". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase "general formula " is recited. The expression of the term "general" is without further clarification by the specification. Therefore, an appropriate correction is required.

In claim 21, the phrase "the group of ketones comprising " is recited. The expression of the term "comprising" is vague and indefinite. The meaning of "ketones comprising" would mean many additional compounds besides the ketones. Therefore, the examiner recommends to change from "comprising " to " consisting of." An appropriate correction is required.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2 and 8-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elango et al (U.S. 4,981,995) in view of Chaudhari et al (U.S. 6,093,847) .

Elango et al discloses a method of preparing ibuprofen by reacting 1-(4'-Isobutylphenyl)ethanol (56.0 mmol), PdCl₂(PPh₃)₂ (0.37 mmol), HCl (68 mmol) and benzene in an autoclave, which is flushed with N₂ and CO before the initiation of the reaction process; the mixture has been heated to 125-129 ° C. at a pressure of 800 psig with CO for 16 h. with stirring. The autoclave has been cooled to room temperature and vented out of CO, and the resultant mixture has been collected. Furthermore, the organic layer of the resultant mixture has got separated from the aqueous layer to isolate the desired product (see col. 10 , lines 10-24).

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In addition, during the carbonylation reaction, water may be added in an amount of 10 to 600 % based on the weight of IBPE (1-(4'-Isobutylphenyl)ethanol) (see col. 3 , lines 24-28) and for other types of solvents, acetonitrile and methyl ethyl ketone can be used as solvent replacements for benzene ,along with cyclic ethers such as tetrahydrofuran and dioxane (see col. 4 , lines 20-27).

For catalysts for the reaction, some palladium complex with an appropriate ligand such as tetrakis(triphenylphosphine) complex may be employed; furthermore, the palladium metal can be placed on a suitable catalyst support such as alumina and silica (see col. 3 , lines 34-52). Also, the mole ratio of palladium to IBPE is in the range of from 1: 150 to 1:30,000 (see col. 3 , lines 64-67) whereas the mole ratio of phosphine to palladium is at least 2:1(see col. 3 , lines 60-63).

Concerning other additives, hydrogen and halide ions may be added. As for the source of halide ions, potassium, sodium, and lithium chlorides, bromides, and iodides can be useful (see col. 4 , lines 1-4) and for the source of hydrogen ions, p-toluenesulfonic acid, methanesulfonic acid are recommended as an alternative to inorganic acids(see col. 4 , lines 5-10) . The mole ratio of hydrogen ions or halide ions to IBPE may be in the range of from 0.15 to 5 (see col. 4 , lines 16-19) whereas the mole ratio of hydrogen ions or halide ions to palladium can be estimated from dividing the mole ratio of hydrogen ions or halide ions to IBPE by the mole ratio of palladium to IBPE: from the lowest value of 22.5 (0.15×150) to the highest one 150,000 ($5 \times 30,000$).

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However, the instant invention differs from the Elango et al in that one of the halide promoters is tetrabutyl ammonium chloride , the water is in the range of 1 to 6 %(v/v) of the total mixture , and the reaction vessel is flushed with an inert gas after the reaction process.

Chaudhari et al discloses a process of preparing ibuprofen by reacting an aryl alcohol with a halide source, such as lithium chloride, or tetrabutyl ammonium chloride(see col. 2, lines 48-51), protonic acid, water (4% v/v) (see col. 4 , example 3), palladium catalyst with a phosphine ligand(see col. 1 ,lines 63-67) in the presence of solvents such as N-methyl-pyrrolidone (see col. 2 ,lines 61-65) in a stirred reactor.

With respect to the reaction vessel being flushed with an inert gas after the reaction process, Elango et al does teach that step before the initiation of the reaction process. It has been held that merely reversing the order of steps in a multi-step process is not a patentable modification absent unexpected or unobvious results. EX parte Rubin, 128 U.S.P.Q. 440 (P.O.B.A. 1959).

Elango et al does disclose the method of preparing ibuprofen by reacting 1-(4'-Isobutylphenyl)ethanol , $\text{PdCl}_2(\text{PPh}_3)_2$, HCl, lithium chloride as a halide source, and benzene in an autoclave at $125\text{-}129^\circ\text{C}$. at a pressure of 800 psig. Chaudhari et al discloses a process of preparing ibuprofen by reacting an aryl alcohol with tetrabutyl ammonium chloride as a halide source , protonic acid, water (4% v/v) palladium

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catalyst with a phosphine ligand in the presence of solvents such as N-methyl-pyrrolidone in a stirred reactor. Both are involved in the common process of preparing ibuprofen. Also, Chaudhari et al expressly indicates that there is an equivalency between tetrabutyl ammonium chloride and lithium chloride as for the halide source. Therefore, it would have been obvious to the skillful artisan in the art to have motivated to use the Chaudhari et al tetrabutyl ammonium chloride as an alternative for lithium chloride. This is because the skilled artisan in the art would expect the incorporation of the Chaudhari et al tetrabutyl ammonium chloride into the Elango et al process to be successful similarly shown in the Chaudhari et al.

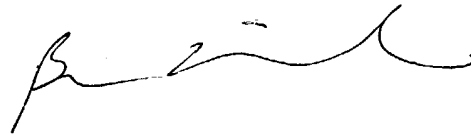
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached from 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Mckane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

vsh
3/20/04



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